IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

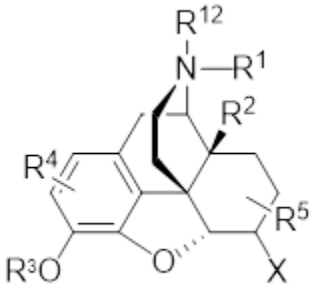
AETHER THERAPEUTICS, INC., Plaintiff, v. ASTRAZENECA AB, ASTRAZENECA PHARMACEUTICALS LP and NEKTAR THERAPEUTICS, Defendants.	)	C.A. No. 20-381 (MN)
AETHER THERAPEUTICS, INC., Plaintiff, v. REDHILL BIOPHARMA, INC., Defendant.	)	C.A. No. 21-248 (MN)

MEMORANDUM ORDER

At Wilmington this 14th day of February 2023:

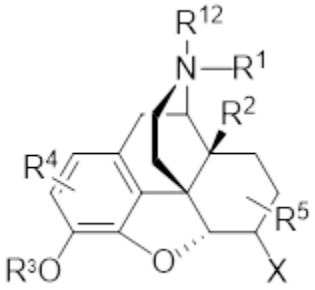
As announced at the hearing on February 3, 2023, IT IS HEREBY ORDERED that the disputed claim term of U.S. Patent No. 6,713,488 ("the '488 Patent") is construed as follows:

1. "naltrexone analog" means a compound with the polycyclic backbone depicted at column 4, lines 15-25:



where permitted substitutions at the R and X groups include but are not limited to those listed at column 4, lines 28-52.

2. "naloxone analog" means a compound with the polycyclic backbone depicted at column 6, lines 1-12:



where permitted substitutions at the R and X groups include but are not limited to those listed at column 6, lines 16-42.[1]

The parties briefed the issues (*see* D.I. 229)[2] and submitted an appendix containing intrinsic and extrinsic evidence, including expert declarations (*see* D.I. 230). The Court carefully reviewed all submissions in connection with the parties' contentions regarding the disputed claim terms,

[1] The Court also found that Defendants had again failed to prove indefiniteness by clear and convincing evidence in these proceedings.

[2] D.I. cites are to docket items in C.A. No. 20-381.

heard oral argument and expert testimony (*see* D.I. 239) and applied the following legal standards in reaching its decision:

I. LEGAL STANDARDS

A. Claim Construction

"[T]he ultimate question of the proper construction of the patent [is] a question of law," although subsidiary fact-finding is sometimes necessary. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 574 U.S. 318, 325-27 (2015). "[T]he words of a claim are generally given their ordinary and customary meaning [which is] the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005) (en banc) (cleaned up). Although "the claims themselves provide substantial guidance as to the meaning of particular claim terms," the context of the surrounding words of the claim also must be considered. *Id.* at 1314. "[T]he ordinary meaning of a claim term is its meaning to the ordinary artisan after reading the entire patent." *Id.* at 1321 (internal quotation marks omitted).

The patent specification "is always highly relevant to the claim construction analysis . . . [as] it is the single best guide to the meaning of a disputed term." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). It is also possible that "the specification may reveal a special definition given to a claim term by the patentee that differs from the meaning it would otherwise possess. In such cases, the inventor's lexicography governs." *Phillips*, 415 F.3d at 1316. "Even when the specification describes only a single embodiment, [however,] the claims of the patent will not be read restrictively unless the patentee has demonstrated a clear intention to limit the claim scope using words or expressions of manifest exclusion or restriction." *Hill-Rom Servs., Inc. v. Stryker Corp.*, 755 F.3d 1367, 1372 (Fed. Cir. 2014) (internal quotation marks omitted) (quoting *Liebel-Flarsheim Co. v. Medrad, Inc.*, 358 F.3d 898, 906 (Fed. Cir. 2004)).

In addition to the specification, a court "should also consider the patent's prosecution history, if it is in evidence." *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996). The prosecution history, which is "intrinsic evidence, . . . consists of the complete record of the proceedings before the PTO [Patent and Trademark Office] and includes the prior art cited during the examination of the patent." *Phillips*, 415 F.3d at 1317. "[T]he prosecution history can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower than it would otherwise be." *Id.*

In some cases, courts "will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period." *Teva*, 574 U.S. at 331. Extrinsic evidence "consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." *Markman*, 52 F.3d at 980. Expert testimony can be useful "to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. Nonetheless, courts must not lose sight of the fact that "expert reports and testimony [are] generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* Overall, although extrinsic evidence "may be useful to the court," it is "less reliable" than intrinsic evidence, and its consideration "is unlikely to result in a reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence." *Id.* at 1318-19. Where the intrinsic record unambiguously describes the scope

of the patented invention, reliance on any extrinsic evidence is improper. *See Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1308 (Fed. Cir. 1999) (citing *Vitronics*, 90 F.3d at 1583).

B. Indefiniteness

"The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, *e.g.* competitors of the patent owner, can determine whether or not they infringe." *All Dental Prodx, LLC v. Advantage Dental Prods., Inc.*, 309 F.3d 774, 779-80 (Fed. Cir. 2002) (citing *Warner-Jenkinson Co. v. Hilton-Davis Chem. Co.*, 520 U.S. 17, 28-29 (1997)). Put another way, "[a] patent holder should know what he owns, and the public should know what he does not." *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co., Ltd.*, 535 U.S. 722, 731 (2002).

A patent claim is indefinite if, "viewed in light of the specification and prosecution history, [it fails to] inform those skilled in the art about the scope of the invention with reasonable certainty." *Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014). A claim may be indefinite if the patent does not convey with reasonable certainty how to measure a claimed feature. *See Teva Pharm. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1341 (Fed. Cir. 2015). But "[i]f such an understanding of how to measure the claimed [feature] was within the scope of knowledge possessed by one of ordinary skill in the art, there is no requirement for the specification to identify a particular measurement technique." *Ethicon Endo–Surgery, Inc. v. Covidien, Inc.*, 796 F.3d 1312, 1319 (Fed. Cir. 2015).

Like claim construction, definiteness is a question of law, but the Court must sometimes render factual findings based on extrinsic evidence to resolve the ultimate issue of definiteness. *See, e.g.*, *Sonix Tech. Co. v. Publications Int'l, Ltd.*, 844 F.3d 1370, 1376 (Fed. Cir. 2017); *see also*

Teva, 574 U.S. at 333-36. "Any fact critical to a holding on indefiniteness . . . must be proven by the challenger by clear and convincing evidence." *Intel Corp. v. VIA Techs., Inc.*, 319 F.3d 1357, 1366 (Fed. Cir. 2003); *see also Tech. Licensing Corp. v. Videotek, Inc.*, 545 F.3d 1316, 1338 (Fed. Cir. 2008).

I. THE COURT'S RULING

The Court's ruling regarding the disputed claim term of the '488 Patent was announced from the bench at the conclusion of the hearing as follows:

> This is the second time that the parties have raised a dispute over the meaning of "naltrexone analog" and "naloxone analog," terms which appear in asserted claims 25, 26 and 29 of the '488 Patent (and all other independent claims of the patent). During the original claim construction proceedings, Plaintiff proposed to construe "analog" as "chemical compound having structural similarity to a referenced compound." Defendants, on the other hand, argued that "naloxone analog" and "naltrexone analog" were the proper terms for construction and, further, that those terms were indefinite. During argument, Plaintiff agreed that "naltrexone analog" and "naloxone analog" were the terms that should be construed. Then, Plaintiff abruptly changed its constructions and began arguing that "naloxone analog" and "naltrexone analog" must be structurally identical to naloxone or naltrexone except for a small subset of permitted substitutions at the C6 carbon. Defendants had never before heard those proposed constructions or supporting arguments. I ultimately declined to reach the indefiniteness issue on the record at the time and also warned Plaintiff that its new constructions seemed at odds with the intrinsic evidence.[3]
>
> Now the parties are back fighting about the construction of "naloxone analog" and "naltrexone analog," and Plaintiff is again pushing effectively the same constructions that it raised during the previous hearing. That is, Plaintiff again contends that "naltrexone analog" is simply naltrexone with a small set of substitutions permissible at the C6 carbon, which is also referred to as the X group in the '488 Patent. And for "naloxone analog," Plaintiff contends that the structure is naloxone with a small set of substitutions permissible at the C6 carbon, again the X group. The permissible X groups in Plaintiff's view are found at column 4, lines 40 through 52, and column 6, lines 29 to 42. Defendants proposed to construe

[3] (*See* D.I. 98 at 57:17-58:24).

the terms to mean "a drug whose structure is related, or analogous in some respect, to the structure of [naltrexone/naloxone]." This is a modified – and broader – rendition of Plaintiff's original proposal. I disagree with both sides.

As to Plaintiff's proposal, I continue to have the same issue today that I did before, namely that Plaintiff is unable to offer intrinsic evidence in support of this narrow set of constructions. Indeed, the intrinsic evidence suggest that "naloxone analog" and "naltrexone analog" as used in the claimed invention are broader than Plaintiff's proposal. For example, the analog terms have the same meaning across the various independent claims – *e.g.*, independent claims 1 and 25. But claim 2, which depends from claim 1, is unquestionably broader than the structure offered by Plaintiff. Claim 2 allows for substitutions beyond the C6 X-group carbon, but Plaintiff maintains that an analog as claimed is naloxone or naltrexone only modified by substitution at the C6 carbon.[4] So I think that Plaintiff's proposal is largely nonsensical in the context of the dependent claims because it would result in claim 2 being far broader than claim 1. Additionally, the specification contemplates broader genuses for the analogs as well. At column 4, lines 11 to 52, "naltrexone analog" is depicted according to a formula with a multi-ring backbone and a number of permissible substitutions at locations other than C6. For example, the various R groups throughout the polycyclic structure can be various alkyl groups, alkoxy groups, halogens, et cetera, depending on the location of the R group – just to name a few examples. The same is true for "naloxone analog" at column 5, line 66 to column 6, line 42. This disclosure further suggests that Plaintiff is attempting to improperly narrow the set of analogs covered by the claims of the '488 Patent. Therefore, Plaintiff's proposal cannot be the correct construction.

As to Defendants' proposal, I am also unpersuaded that it is the proper construction of the analog terms. Defendants' proposal goes even beyond the original construction offered by Plaintiff in the first round of claim construction – *i.e.*, Defendants argue an analog is "a drug whose structure is related, or analogous in some respect, to the structure" of either naloxone or naltrexone. Apart from the fact that this construction seems to be crafted to fall within

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4 At the hearing and in response to questions from Defendants and the Court, Plaintiff's expert agreed that his construction of analog required the identical structure of naltrexone or naloxone with only a limited set of modifications permitted at the C-6 X-group position. (*See, e.g.*, D.I. 239 at 41:17-21 & 45:11-46:9; *see id.* at 46:6-9 ("Q. In order to have a naltrexone analog under your construction, you have to have a cyclopropyl group there [at the R^1 position]? A. Yes.")).

an indefiniteness challenge, it ignores the intrinsic evidence that I just discussed and which supplies some concrete structure to the meaning of naloxone and naltrexone analogs – namely, the polycyclic backbone.

In the end, I think that the constructions of "naltrexone analog" and "naloxone analog" that stay truest to intrinsic evidence are ones that incorporate the polycyclic backbone of naltrexone and naloxone. Starting with the plain meaning of analog on its own, a POSA would understand that to mean related structure to another chemical compound. For that I will cite the IUPAC definition of "analog."[5] As to analogs of naltrexone and naloxone specifically, as I have already discussed, the '488 Patent discusses genuses in the "Summary of Invention." At column 4, lines 11 to 25, the specification provides that "naltrexone analogs suitable for use in the invention can be represented by Formula I and include the pharmaceutically acceptable salts thereof" and is followed by a depiction of the polycyclic backbone of naltrexone with various R groups and an X group at the C6 carbon. The specification further provides permissible substitutions at those R and X groups at column 4, lines 27 through 52. The specification does the same for "naloxone analog" at column 5, line 66 to column 6, lines 1 to 42. In fact, the depiction of structure for a "naloxone analog" is the same structure depicted for the "naltrexone analog" in column 4. Based on this disclosure in the "Summary of Invention," I think that the claimed analogs of the present invention must include the polycyclic backbone depicted for both "naltrexone analogs" and "naloxone analogs" along with R and X groups as well. This is actually consistent with the rest of the patent in terms of structure for the claimed analogs. I do not think, however, that a person of ordinary skill reading the intrinsic evidence would understand the substitutions permissible at the R and X groups to only be those specifically listed in the specification. There is nothing in the specification that indicates only these substitutions are allowed for a compound to be considered an analog. In fact, comparing the scope of dependent claim 2, which is coextensive with the disclosure in the "Summary of Invention," to the scope of claim 1 suggests that the naltrexone and naloxone analogs of claim 1 must be broader so that the two claims are of different scope.

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5 (D.I. 230 at Appx0057 ("An analog is a drug whose structure is related to that of another drug but whose chemical and biological properties may be quite different."); *see also* D.I. 239 at 32:4-18 (Plaintiff's expert agreeing that IUPAC is a trusted source for definitions in the field)).

> The prosecution history also suggests that other non-listed substitutions are permissible and still result in a compound that the Applicant considered a "naltrexone analog" or "naloxone analog." In response to the only office action, the Applicant specifically agreed with the Examiner that "nalmefene is a structural and pharmaceutical analog of naltrexone."[6] It is undisputed that the only difference structurally between nalmefene and naltrexone is the C6 X group has been changed from a ketone to an ethylene group. But an ethylene group is not one of the permitted substitutions for the C6 carbon listed in column 4, lines 40 to 52. Under Plaintiff's proposal today, however, nalmefene would not be a "naltrexone analog" because the C6 carbon substitution is not one of the ones permitted in column 4 – but that flies in the face of what the Applicant said to the Examiner. This further suggests that Plaintiff's current construction of "naltrexone analog" and "naloxone analog" is unduly narrow and contrary to the intrinsic evidence.
>
> I will note that Applicant then went on to distinguish nalmefene from the present invention on the basis that it is not a neutral antagonist at the μ-opioid receptor, which relates to a separate claim limitation that follows the analog term. Plaintiff also makes much of this argument in its claim construction positions today – *i.e.*, arguing that only C6 substitutions are permitted because only those can give rise to neutral antagonism at the μ receptor. I think that that is irrelevant to the construction of "naltrexone analog" and "naloxone analog" because there is a separate limitation recited in the claims that also requires the analog to be a neutral antagonist at the μ receptor.[7]
>
> So in sum, I will construe "naltrexone analog" and "naloxone analog" to mean a compound with the polycyclic backbone depicted at column 4, lines 11 to 25 [for naltrexone analog] and column 6, lines 1 through 11 [for naloxone analog] where permitted substitutions at the R and X groups include but are not limited to those listed in columns 4 to 6 of the '488 Patent [for each analog]. I will also include a depiction of this in my order.

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6 (D.I. 230 at Appx0050).

7 Indeed, Plaintiff's expert agreed that there are two separate inquiries under the claims. (*See* D.I. 239 at 30:8-17 ("Q. For an administered drug to fall within the asserted claims, it has to meet both a structural requirement as well as a functional requirement; correct? A. Yes. Q. The structural requirement in these claims is found in the analog limitations? A. Yes. Q. And the functional requirement in these claims is found in the neutral antagonist limitation? A. It is.")).

Further as to definiteness, Defendants' argument seems to suggest that use of the term analog without specific boundaries results in indefiniteness. I cannot square that position with caselaw that construes such terms to be definite,[8] as well as the fact that I think even Defendants' expert recognized that the term "analog" is used in patents, and I think from our review even in AstraZeneca's own patents. And in the end, I do not think that Defendants have met their burden to prove by clear and convincing evidence that the claims are invalid for indefiniteness.

Maryellen Noreika

The Honorable Maryellen Noreika
United States District Judge

8 *See, e.g.*, *Bos. Sci. Corp. v. Johnson & Johnson Inc.*, 679 F. Supp. 2d 539, 554 (D. Del. 2010), *aff'd*, 647 F.3d 1353 (Fed. Cir. 2011).